REMARKS

Applicants respectfully request consideration of the foregoing claim amendments and following comments upon continued examination of the present application.

I. Status of the Claims

Claims 4, 5, 9-15, 17, 53, 54, 58-63, 73-86 and 89 were cancelled previously. Claims 101-105 are added with exemplary support in the original claims. Because no new matter is introduced, Applicants respectfully request entry of this amendment. Upon entry, claims 1-3, 6-8, 16, 18-52, 55-57, 64-72, 87, 88 and 90-105 are pending, with claims 26-49 withdrawn from examination. Applicants respectfully request that the withdrawn claims directed to methods of making the claimed compositions be rejoined for examination upon allowance of the corresponding product claims.

II. Rejection of Claims under 35 U.S.C. §103(a)

A. Struengmann and Liversidge

Claims 1-3, 6-8, 16, 50-52, 55-57, 64-67, 87, 88 and 90-97 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over PCT Publication No. WO 99/09988 by Struengmann et al. ("Struengmann"), in view of PCT Publication No. WO 93/25190 by Liversidge et al. ("Liversidge"). Applicants respectfully traverse the rejection.

The Examiner asserts that the claimed invention is obvious over the cited art because one skilled in the art would have considered it obvious to modify the micronized meloxicam composition of Struengmann in view of the process of Liversidge to obtain the claimed invention. *See* final Office Action, pages 3 and 4.

(i) There is no reason to modify Struengmann's composition in view of Liversidge.

The Examiner's identified reasons to combine the teachings of the references are that: (a) Struengmann teaches reduction of particles size of meloxicam by micronization, and (b) Liversidge teaches a process to improve rapid onset (bioavailability). *See* final Office Action, page 4, 1st full paragraph.

First, Struengmann's teaching, when taken as a whole, describes improving bioavailability by increasing the solubility of meloxicam. Struengmann disclosed that when a number of additives are mixed with meloxicam, the solubility of meloxicam is increased, as evidenced by the meloxicam dissolution data in the working examples. Although there is a very brief mention that meloxicam is micronized in the presence of co-solvents and hydrotropic agents, Struengmann fails to establish any correlation between particle size reduction and improving bioavailability. In other words, Struengmann does not teach that reducing the particle size of meloxicam may contribute to improving the solubility and bioavailability of meloxicam. This is evidenced by the absence of any disclosure regarding the particle size of meloxicam for Struengmann's composition and the lack of any suggestion that the meloxicam particle size should be reduced to achieve better solubility and bioavailability. Therefore, the Examiner's rejection premised on Struengmann's alleged teaching of reducing the meloxicam particle size to improve solubility and bioavailability lacks valid support in the cited reference.

Second, the proposed goal of improving the bioavailability of meloxicam is already achieved by Struengmann's teaching regarding mixing meloxicam with additives to increase the solubility of meloxicam. The skilled artisan would not have any reason to look to the secondary reference, Liversidge, to tackle a problem already solved by the primary reference. *See* the Decision on Appeal, *Ex Parte Rinkevich* (Appeal No. 2007-1317 decided on May 29, 2007). In *Rinkevich*, the Board concluded that the Examiner incorrectly asserted that an artisan would have looked to Wu (the secondary reference) to solve the purported deficiencies of Savill (the primary

reference) because "a person of ordinary skill in the art having common sense at the time of the invention would not have reasonably looked to Wu to solve a problem already solved by Savill" (the paragraph bridging pages 8 and 9). In the present case, the skilled artisan would not have any reason, in the absence of the teaching of Applicants' claimed invention, to improve the bioavailability of meloxicam because Struengman teaches that the bioavailability of meloxicam has already been improved to a satisfactory level by mixing meloxicam with additives to increase the solubility of the drug.

(ii) Even when the teachings of Struengman and Liversidge are combined, Applicants' claim limitations of certain surface stabilizers are not met.

As discussed in the accompanying Declaration under Rule 1.132 executed by Dr. Gary Liversidge, neither Struengman nor Liversidge have any teachings regarding selecting the specific surface stabilizers, polyvinylpyrrolidone and/or sodium deoxycholate, prescribed by claims 1 and 104. Furthermore, neither reference teaches sodium dexoycholate as an ingredient for the composition. *See* the Liversidge Declaration, paragraphs 8-10 and 12. This is significant because these surface stabilizers are highly preferred, as taught by the Liversidge Declaration. *See also* Section II.A.(iii), below. Accordingly, even if the skilled artisan would have any reason to combine the cited references, the claimed invention as prescribed by claims 1 and 104 would not be obtained.

(iii) The claimed invention is nonobvious in view of the unexpected results.

As demonstrated in the Liversidge Declaration, the claimed meloxicam compositions unexpectedly exhibited superior stability. *See* paragraph 13 and Table 1. In addition to the physical stability of the claimed meloxicam compositions, the outstanding *in vivo* bioavailability of the claimed nanoparticulate meloxicam compositions, in comparison to the commercial, microparticulate meloxicam formulation, MOBIC®, is demonstrated by trials in dog models and by human clinical trials. *See* paragraphs 14-16, and Tables 2 and 3.

Moreover, due to the small particle size of meloxicam provided by the claimed invention, meloxicam is able to be formulated into an intravenous injectable formulation. This is in contrast to the prior art meloxicam formulation, MOBIC®, which was only available in oral dosage forms. This is significant because an injectable formulation has the fastest onset among different dosage forms. This is a significant and very important achievement in drug formulation for meloxicam, which is prescribed as a pain reliever. Additionally, the claimed invention provides an alternative administration route to a patient population who cannot take drugs in oral dosage form.

In view of the foregoing, Applicants respectfully request that the rejection under 35 U.S.C. §103(a) be withdrawn.

B. Struengman, Liversidge, Desai and Courteille

Claims 18-25, 68-72 and 98-100 are rejected under 35 U.S.C. §103(a) for allegedly being obvious over Struengmann, in view of Liversidge, and further in view of PCT Publication No. WO 01/45706 by Desai et al. ("Desai") and U.S. Patent No. 5,384,124 to Courteille et al. ("Courteille"). Applicants respectfully traverse the rejection.

The teachings of Struengmann and Liversidge are discussed *supra*. Desai and Courteille are cited for allegedly teaching a second particle population but fail to remedy the deficiencies of Struengmann and Liversidge. Accordingly, the dependent claims are nonobvious for depending from nonobvious base claims, and further in view of the unexpected results demonstrated by the Liversidge Declaration.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the

undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By 

FOLEY & LARDNER LLP
Customer Number: 31049
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicant
Registration No. 34,717